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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 1 of 3

Complete if Known

Application Number	09/808,832
Filing Date	March 15, 2001
First Named Inventor	Copeland et al
Group Art Unit	16534
Examiner Name	J. Russell - Russe
Attorney Docket Number	PH-7134

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
JRL	AA	5,962,216		Trouet et al	10/5/1999	435/4
JRL	AB	4,703,107		Monsigny et al	10/27/1987	530/330
JRL	AC	6,342,480		Trouet et al	1/29/2002	514/18

FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM- DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T 6
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
JRL		WO	9600503		Merck & Co. Inc.	1/11/1996		
JRL		WO	9605863		La Region Wallonne	2/29/1996	See AA & AC	
JRL		WO	9712624		Merck & Co. Inc.	4/10/1997		
JRL		WO	9714416		Merck & Co. Inc.	4/24/1997		
JRL		WO	9748725		Peptech Limited	12/24/1997		
JRL		WO	9810651		Merck & Co. Inc.	3/19/1998		
JRL		WO	9810795		Burnham Inst.	3/19/1998		
JRL		WO	9816240		Liposome Co. Inc.	4/23/1998		
JRL		WO	9818493		Merck & Co. Inc.	5/7/1998		
JRL		WO	9846250		The Regents of the Univ. of CA	10/22/1998		
JRL		WO	9902175		Merck & Co. Inc.	1/21/1999		
JRL		WO	0033888		Coulter Pharmaceutical, Inc.	6/15/2000		
JRL		WO	0059930		Merck & Co. Inc.	10/12/2000		
JRL		WO	0064486	✓	Veritas Medical Techn., Inc.	11/2/2000		
JRL		WO	0071571		Boehringer Ingelheim	11/30/2000		
JRL		EP	126685		Centre National de la Recherche Scientifique	11/28/1984	See AB	
JRL		EP	359347		Neorx Corporation	3/21/1990		
JRL		UK	2131813	✓	Monsanto Co.	6/27/1984		
Examiner Signature		Jeffrey E. Russell				Date Considered	December 3, 2002	

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Sheet 2 Of 3

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Application Number	09/808,832
Filing Date	March 15, 2001
First Named Inventor	Copeland et al
Group Art Unit	16524
Examiner Name	J. Russell Russell
Attorney Docket Number	PH-7134

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
JR	1	TIMAR et al, "The antiproliferative action of a melphalan hexapeptide with collagenase-cleavable site" Cancer Chemotherapy Pharmacology, vol. 41, no. 4, 1998, 292-298	2
JR		MASQUELIER et al, "Amino Acid and Dipeptide Derivatives of Daunorubicin. 1. Synthesis, Physicochemical Properties, and Lysosomal Digestion", Journal of Medicinal Chemistry, American Chemical Society, vol. 23, no. 11, 1980, 1166-1170.	
JR		DENMEADE et al, "Enzymatic Activation of a Doxorubicin-Peptide Prodrug by Prostate-Specific Antigen", Cancer Research, American Assoc. for Cancer Research, vol. 58, June 15, 1998, 2537-2540	
JR		SAFAVY et al, "Paclitaxel Derivatives for Targeted Therapy of Cancer: Toward the Development of Smart Taxanes" Journal of Medicinal Chemistry, Am. Chem. Soc., vol. 42, 1999, 4919-4924	
JR		MCGEEHAN et al, "Characterization of the Peptide Substrate Specificities of Interstitial Collagenase and 92-KDA Gelatinase Implications of Substrate Optimization" Journal of Biological Chem., vol. 269, no 52, Dec. 30, 1994, 32814-32820	
JR		AIMES et al, Matrix Metalloproteinase-2 Is an Interstitial Collagenase, Journal of Biological Chemistry, vol. 270, No. 11, March 17, 1995, 5872-5876, 1995	
JR		KURCHAT et al, Tissue Inhibitor of Matrix Metalloproteinase-2 Regulates Matrix Metalloproteinase-2 Activation by Modulation of Membrane-type 1 Matrix Metalloproteinase Activity in High and Low Invasive Melanoma Cell Lines, Journal of Biological Chemistry, vol. 274, No. 30, 21056-21062, 1999	
JR		GARBISA et al, Correlation of Serum Metalloproteinase Levels with Lung Cancer Metastasis and Response to Therapy, Cancer Research, 52, 4548-4549, 1992	
JR		BOVEN et al, Doxorubicin Compared with Related Compounds in a Nude Mouse Model for Human Ovarian Cancer, Eur. J. Cancer, Vol. 26, no. 9, 983-986, 1990	
JR		KNAUPER et al, Biochemical Characterization of Human Collagenase-3, Biological Chemistry, Vol. 271, No. 3, 1544-1550, 1996	
JR		BROOKS et al, Localization of Matrix Metalloproteinase MMP-2 to the Surface of Invasive Cells by Interaction with Integrin $\alpha\beta 3$, Cell, Vol. 85, 683-693, 1996	
JR		MOSES et al, Increased Incidence of Matrix Metalloproteinases in Urine of Cancer Patients, Cancer Research, 58, 1395-1399, 1998	
JR		CANAL et al, Human pharmacokinetics of N-L-leucyl-doxorubicin, a new anthracycline derivative, and its correlation with clinical toxicities, Clin. Pharmacol. Ther., volume 51, number 3, 249-259, 1992	
JR		BOVEN et al, The anti-tumour effects of the prodrugs N-L-leucyl-doxorubicin and vinblastine-isoleucinate in human ovarian cancer xenografts, Br. J. Cancer, 66, 1044-1047, 1992	
Examiner Signature	Jeffrey E. Russell		Date Considered December 3, 2002

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Examiner Name	J. Russell (Rus. Jc.)
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JRL		MCDONNELL et al, Role of matrix metalloproteinases in invasion and metastasis: biology, diagnosis and inhibitors, Cytotechnology, 12, 367-384, 1993	
JRL		BRUMMER et al, Matrix-metalloproteinases 1, 2 and 3 and their tissue inhibitors 1 and 2 in benign and malignant breast lesions: an in situ hybridization study, Virchows Arch, 435, 566-573, 1999	
JRL		MACDOUGALL et al, Contributions of tumor and stromal matrix metalloproteinases to tumor progression, invasion and metastasis, Cancer and Metastasis Reviews, 14, 351-362, 1995	
JRL		DE JONG et al, Plasma Pharmacokinetics and Pharmacodynamics of a New Prodrug N-I-Leucyldoxorubicin and Its Metabolites in a Phase I Clinical Trial, Journal of Clinical Oncology, vol. 10, no. 12, 1897-1906, 1992	
JRL		DE GROOT et al, Synthesis and Biological Evaluation of Novel Prodrugs of Anthracyclines for Selective Activation by the Tumor-Associated Protease Plasmin, J. Med. Chem., 42, 5277-5283, 1999	
		SAFAVY et al, Paclitaxel Derivatives for Targeted Therapy of Cancer: Toward the Development of Smart Taxanes, J. Med. Chem., 42, 4919-4924, 1999	
JRL		NAGASE et al, Human Matrix Metalloproteinase Specificity Studies Using Collagen Sequence-Based Synthetic Peptides, Biopolymers, vol. 40, 399-416, 1996	
JRL		WHITTAKER et al, Design and Therapeutic Application of Matrix Metalloproteinase Inhibitors, Chem. Rev. 99, 2735-2776, 1999	

Examiner
Signature

Jeffrey E. Russell

Date
Considered

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